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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,789	12/30/2003	Mark A. Conkling	5051-338CTDV	9424
20792	7590	10/04/2006	EXAMINER	
MYERS BIGEL SIBLEY & SAJOVEC			KALLIS, RUSSELL	
PO BOX 37428			ART UNIT	
RALEIGH, NC 27627			PAPER NUMBER	

1638

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/748,789

Applicant(s)

CONKLING ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 63-93 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 63-93 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/05;5/06;12/04;12/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Priority

The reference to priority applications at the beginning of the specification should be amended to indicate that Application 09/021,286 is now U.S. Patent 6,586,661.

Claim Rejections - 35 USC § 112

Claims 63-71, 73-74, 76-88, 90-91 and 93 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method of increasing the expression of QPRTase in a transformed plant cell and plant; and a plant thereby.

Applicants describe SEQ ID NO: 1 encoding a quinolinate phosphoribosyltransferase of SEQ ID NO: 2 from *N. tabacum*; and QPRTase sequences from bacteria *E. coli* and *S. typhimurium*.

Applicants do not describe a representative number of sequences that share all the conserved regions of SEQ ID NO: 1 or SEQ ID NO: 2 and that encode a QPRTase.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial

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portion of the genus.” See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of DNA sequence that encode QPRTase. Applicants only describe a quinolinate phosphoribosyltransferase of SEQ ID NO: 2 from *N. tabacum*; and QPRTase sequences from bacteria *E. coli* and *S. typhimurium*. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of QPRTase sequences. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for QPRTase activity, it remains unclear what features identify a QPRTase. Since the genus of DNA sequence encoding QPRTases has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Claims 63-93 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior

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art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are broadly drawn to a method of increasing the expression of QPRTase in a transformed plant cell and plant; and a plant thereby.

Applicants provide guidance for constructing antisense constructs using the isolated QPRTase from *tabacum* for the antisense inhibition of QPRTase expression in *N. tabacum* transformed with full length antisense of SEQ ID NO: 1 (specification pages 26-28).

Applicants do not teach overexpression of QPRTase in any species of plants or constructs for said transformation or any detectable phenotype in plants overexpressing QPRTase.

The state-of-the-art does not recognize that non-plant QPRTase encoding sequences would function in a similar fashion as the endogenous QPRTase sequences. The sequence comparison of bacterial and plant QPRTase enzyme sequences shows that the bacterial QPRTases lack a N-terminal peptide sequence that has been identified as a mitochondrial targeting sequence. The evidence suggests that nicotine biosynthesis would require a N-terminal sequence found on the *N. tabacum* sequence, and thus bacterial sequences would not function in a plant system because they would not be expressed in the correct plant subcellular location (Sinclair S. *et al.*, Plant Molecular Biology, 2000, Vol. 44; pp. 603-617; see Discussion especially page 613 column 2 to page 614 column 1).

The state-of-the-art is such that one of skill in the art cannot predict that overexpression of any QPRTase, plant or non-plant would result in a consistent phenotype when transformed into any one of a species of plants that express a sequence encoding QPRTase. Not all species of *Nicotiana* produce the same alkaloid in the same plant tissue in response to overexpression of

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QPRase induced by wounding strongly suggesting that there is divergence among *Nicotiana* in the regulation and tissue specific expression of QPRase and hence alkaloid biosynthesis (Sinclair S. *et al.*, Functional Plant Biology, 2004, Vol. 31; pp. 721-729; see page 726 column 2 to end of article).

Given the lack of guidance in the instant specification, undue trial and error experimentation would be required for one of ordinary skill in the art to test a myriad of plant species for QPRase expression prior to transformation with anyone of a multitude of unspecified QPRase sequences and then test a multitude of divergent plant species for a non-exemplified phenotype indicative overexpression of QPRase.

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 73, 75, 77-78, 90 and 93 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 73, 90 and 93 recite the limitation "the DNA sequence of Claim 1" in line 3. There is insufficient antecedent basis for this limitation in the claim. Claim 1 has been canceled. Moreover, Claim 63 does not recite any DNA sequence in the plural. Further, Claim 63 already recites a DNA sequence encoding a QPRase making claims 73, 90 and 93 redundant.

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Claims 75 and 77-78 recite the limitation "The method according to claim 74" in line 1.

There is insufficient antecedent basis for this limitation in the claim. Claim 74 is a product claim.

All claims are rejected.

The claims are deemed free of the prior art given the failure of the prior art to teach or reasonably suggest a method of increasing QPRTase expression in a plant cell or plant or plants transformed therewith.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Russell Kallis Ph.D.
September 28, 2006

RUSSELL P. KALLIS, PH.D.
PRIMARY EXAMINER

Russell Kallis